

Preferably, GLUTX selective antibodies of the invention are produced using fragments of the GLUTX polypeptide that lie outside highly conserved regions and appear likely to be antigenic, by criteria such as high frequency of charged residues. Fig. 4 includes a graph of the antigenicity index (Jameson-Wolf) for GLUTX. This information can be used to design antigenic peptides. Cross-reactive anti-GLUTX antibodies are produced using a fragment of GLUTX that is conserved amongst members of this family of proteins. In one specific example, such fragments are generated by standard techniques of PCR, and are then cloned into the pGEX expression vector (Ausubel *et al.*, *supra*). Fusion proteins are expressed in *E. coli* and purified using a glutathione agarose affinity matrix as described in Ausubel, *et al.*, *supra*.

In some cases it may be desirable to minimize the potential problems of low affinity or specificity of antisera. In such circumstances, two or three fusions can be generated for each protein, and each fusion can be injected into at least two rabbits. Antisera can be raised by injections in a series, preferably including at least three booster injections.

Antiserum is also checked for its ability to immunoprecipitate recombinant GLUTX polypeptides or control proteins, such as glucocorticoid receptor, CAT, or luciferase.

The antibodies can be used, for example, in the detection of GLUTX in a biological sample as part of a diagnostic assay or to reduce GLUTX activity as part of a therapeutic regime (e.g., to reduce an undesirable level of GLUTX activity). Antibodies also can be used in a screening assay to measure the effect of a candidate compound on expression or localization of GLUTX. Additionally, such

antibodies can be used in conjunction with the gene therapy techniques. For example, they may be used to evaluate the normal and/or engineered GLUTX-expressing cells prior to their introduction into the patient.

5 In addition, techniques developed for the production of "chimeric antibodies" (Morrison *et al.*, *Proc. Natl. Acad. Sci. USA* 81:6851, 1984; Neuberger *et al.*, *Nature* 312:604, 1984; Takeda *et al.*, *Nature* 314:452, 1984) by splicing the genes from a mouse antibody molecule of appropriate antigen  
10 specificity together with genes from a human antibody molecule of appropriate biological activity can be used. A chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a  
15 human immunoglobulin constant region.

Alternatively, techniques described for the production of single chain antibodies (U.S. Patent Nos. 4,946,778, 4,946,778, and 4,704,692) can be adapted to produce single chain antibodies against a GLUTX polypeptide,  
20 or a fragment thereof. Single chain antibodies are formed by linking the heavy and light chain fragments of the Fv region via an amino acid bridge, resulting in a single chain polypeptide.

Antibody fragments that recognize and bind to  
25 specific epitopes can be generated by known techniques. For example, such fragments include but are not limited to F(ab')<sub>2</sub> fragments that can be produced by pepsin digestion of the antibody molecule, and Fab fragments that can be generated by reducing the disulfide bridges of F(ab')<sub>2</sub>  
30 fragments. Alternatively, Fab expression libraries can be constructed (Huse *et al.*, *Science* 246:1275, 1989) to allow rapid and easy identification of monoclonal Fab fragments with the desired specificity.

Antibodies can be humanized by methods known in the art. For example, monoclonal antibodies with a desired binding specificity can be commercially humanized (Scotgene, Scotland; Oxford Molecular, Palo Alto, CA). Fully human  
5 antibodies, such as those expressed in transgenic animals are also features of the invention (Green *et al.*, *Nature Genetics* 7:13-21, 1994; see also U.S. Patent Nos. 5,545,806 and 5,569,825).

The methods described herein, in which anti-GLUTX  
10 antibodies are employed, can be performed, for example, by utilizing pre-packaged diagnostic kits comprising at least one specific antibody reagent described herein, which may be conveniently used, for example, in clinical settings, to diagnose patients exhibiting symptoms of the disorders  
15 associated with aberrant expression of GLUTX.

#### **V. Antisense Nucleic Acid Molecules**

Treatment regimes based on an "antisense" approach involve the design of oligonucleotides (either DNA or RNA)  
20 that are complementary to a portion of a selected mRNA. These oligonucleotides bind to complementary mRNA transcripts and prevent their translation. Absolute complementarity, although preferred, is not required. A sequence "complementary" to a portion of an RNA molecule, as  
25 referred to herein, is a sequence having sufficient complementarity to hybridize with the RNA, forming a stable duplex; in the case of double-stranded antisense nucleic acids, a single strand of the duplex DNA can be tested, or triplex formation can be assayed. The ability to hybridize  
30 will depend on both the degree of complementarity and the length of the antisense nucleic acid. Generally, the longer the hybridizing nucleic acid, the more base mismatches with an RNA it may contain and still form a stable duplex (or